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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,704	12/04/2003	Volkmar Guenzler-Pukall	FP0602.1 US	5297

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EXAMINER	
TELLER, ROY R	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
06/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,704	GUENZLER-PUKALL ET AL.	
	Examiner	Art Unit	
	Roy Teller	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the reply, received 3/26/07.

Claims 1-37 are under examination.

Response to Amendments/ Arguments

Applicant's arguments filed 3/26/07 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed tothe Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register,

Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, that of stabilizing the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There are no species of the claimed genus disclosed that is within the scope of the claimed genus . The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses all function without structure that are not further described. There is substantial variability among the species.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises the stabilizing the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

The written description requirement for a claimed genus may be satisfied through sufficient drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus and subgenera of proteins to be used in the claimed composition. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish the proteins in the genus from others are missing from the disclosure. The specification and claims do not provide any description of what other changes should be made. There is no description of the other sites (other than those which applicant has possession of) at which variability may be tolerated and there is no information regarding the relation of structure

to function. The general knowledge and level of those skilled in the art does not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would not reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus or each subgenus.

The specification does not "clearly allow persons of skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

All other claims depend directly or indirectly from the rejected claim and are, therefore, also rejected under 35 USC 112, first paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

Claims 1-37 are/ stand rejected under 35 USC 102 (b) for the reasons of record which are restated below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Muller (EP 0878 480).

The instant claims are drawn to a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits hydroxylation of hypoxia inducible factor α (i.e., HIF α).

Muller teaches a method to stabilize HIF alpha in an individual via injecting a compound (i.e., iron chelator a or a'-dipyridyl (i.e., DPY)) to inhibit prolyl-4- hydroxylase (Column 4, Lines 49-54; Column 9, Lines 45-48) which is manisfested as inhibiting basal membrane formation induced by a lesion of neuronal tissue. Thus, Muller intrinsically teaches that inhibiting prolyl-4-hydroxylase enzyme stabilizes HIF-alpha in an individual. Muller also teaches that said inhibitor of prolyl-4- hydroxylase to inhibit formation of basal membrane is administered locally to neuronal tissue, intraventricularly, systemically, intravenously, or orally to prevent/inhibit basal membrane formation induced by a lesion of neuronal tissue (Column 2,

Line 8 to Column 11, Line 2). Note that inhibition of said enzyme would intrinsically stabilize the alpha subunit of hypoxia inducible factor (i.e., HIF alpha); because the prior art method teaches inhibition of same enzymes as is recited in instantly claimed invention. (i.e., administering a preparation that for e.g., inhibits lysyl and prolyl–4- hydroxylases enzymes) to stabilize HIF alpha. Furthermore, the prior art methods teach inhibition of said enzymes under *in vitro*, and also under *in vivo* conditions in an animal/mammal/human by administering an inhibitor for said enzyme. Note further that since HIF alpha is stabilized with an inhibitor of prolyl-4- hydroxylase, the prior art methods intrinsically teach a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits HIF α via inhibiting inhibiting HIF α, any of the HIF α, or 2-oxoglutarate dioxygenease enzyme claimed instantly.

Therefore, the reference is deemed to anticipate the instant claims.

Applicant's arguments were carefully considered but were not found persuasive. Applicant contends that the Muller reference teaches inhibition of collagen prolyl-4-hydroxylase, not a HIF hydroxylase enzyme. Applicant states that collagen prolyl-4-hydroxylase and HIF hydroxylases have different substrates, a procollagen chain and a HIF alpha subunit, respectively. Therefore, inhibiting collagen prolyl-4-hydroxylase is not equivalent to inhibiting HIF hydroxylase activity, nor would inhibiting collagen prolyl-4-hydroxylase stabilize the alpha subunit of HIF. However, the examiner contends that Muller teaches an inhibitor of amino acids hydroxylases, such as prolyl-4-hydroxylase, see column 10, claim 4. Said compound is also an inhibitor for HIF prolyl hydroxylase, wherein said HIF prolyl hydroxylase is a procollage prolyl-

4-hydroxylase, as specifically contemplated by applicant (see, instant specification, page 16, paragraph 0064). Further, since HIF alpha is stabilized with an inhibitor of prolyl-4-hydroxylase, the prior art methods intrinsically teach a method to stabilize the alpha subunit of hypoxia inducible factor α (i.e., HIF α) in a subject via administering to said subject a compound that inhibits HIF α via inhibiting inhibiting HIF α. The method steps instantly claimed are the same and therefore inherent-especially in regard to prevention.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is 571-272-0971. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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